IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AVENTIS PHARMACEUTICALS INC. and SANOFI-AVENTIS US LLC,	)	
Plaintiffs,	)	C.A. No. 06-286-GMS
v.	)	
BARR LABORATORIES, INC.,	)	
Defendant.	)	

PLAINTIFFS' PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

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I. INTRODUCTION

1. Plaintiffs Aventis Pharmaceuticals Inc. and Sanofi-Aventis US LLC (collectively, "Aventis") have shown at trial that Defendant Barr Laboratories, Inc. infringed claim 6 of U.S. Patent No. 5,976,573 ("the '573 patent") and claim 26 of U.S. Patent No. 6,143,329 ("the '329 patent") by filing an Abbreviated New Drug Application ("ANDA") for a generic version of Aventis's Nasacort® AQ nasal spray. Like Nasacort® AQ, Barr's ANDA product is odorless, thixotropic, and deposits on the entire nasal mucosa to treat allergic rhinitis and thus infringes.

2. Barr has failed to show by clear and convincing evidence that the asserted claims are anticipated, obvious, or not enabled. Aventis's clinical trials were not a public use because they were tightly controlled; Barr failed to apply the proper test for obviousness (and the evidence shows the claimed invention was not obvious); and Positron Emission Tomography ("PET") studies from before the time of filing showed that the patents' specification described a product that met all of the limitations of the asserted claims.

II. BARR'S ANDA PRODUCT INFRINGES CLAIM 6 OF THE '573 PATENT AND CLAIM 26 OF THE '329 PATENT

3. Under 35 U.S.C. § 271(e)(2)(A), it is an act of infringement to file an ANDA for a drug claimed in a patent (or the use of which is claimed in a patent) in order to market the drug before the expiration of the patent. *Abbott Labs. v. Torpharm, Inc.*, 503 F.3d 1372, 1378 (Fed. Cir. 2007). To prove infringement in this case, Aventis must show by a preponderance of the evidence that every element of the asserted claims is found in Barr's ANDA product, which is compositionally identical to Aventis' Nasacort® AQ product (Tr. 256, 516; PTX 48, 461). *Smithkline Diagnostics, Inc. v. Helena Labs. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988); *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29 (1997).

4. To establish direct infringement of claim 6 of the '573 patent, Aventis is required only to

show that each element is found in Barr's ANDA product. 35 U.S.C. § 271(a).

5. Barr infringes claim 26 under 35 U.S.C. § 271(b) and (c). To establish inducement to infringe claim 26 of the '329 patent, Aventis must show that (1) Barr's package insert includes the directions that, if followed, would induce another party to commit infringing acts; and (2) Barr knew or should have known that its package insert would induce actual infringement.[1] 35 U.S.C. § 271(b); *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 553 (Fed. Cir. 1990). Moreover, the law requires only that Barr's inducing activity results in infringement at least part of the time. *See Purdue Pharma, L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420, 439 (D. Del. 1999) (J. Farnan) (finding inducement when the claimed method of treating pain was practiced by "some," but not all, patients who took the drug); *Alcon Lab., Inc. v. Bausch & Lomb, Inc.*, 52 U.S.P.Q. 2d 1927, 1934 (N.D. Tex. 1999) (finding inducement even though "the vast majority of uses" were noninfringing).

A. Barr Does not Contest that its ANDA Product has Most of the Claim Elements

6. The parties have already agreed that most of the elements of the asserted claims are found in Barr's ANDA product. (D.I. 163 (Appendix A)). The evidence of infringement for some of the remaining claim terms (relating to the odorlessness and unsheared and sheared viscosities of Barr's ANDA product) was undisputed. The remaining disputed terms for claim 6 of the '573 patent were: (i) "flows readily into the nasal passages for deposit on the mucosal surfaces of the nasal cavity," and (ii) "in deposited form on the mucosal surfaces, the viscosity of the composition is about 400 to about 800 cp and such that it resists being cleared from the mucosal surfaces by the inherent mucociliary forces which are present in the nasal cavity." The disputed terms for claim 26 of the '329 patent were: (i) "thixotropic," (ii) "to each of the mucosal surfaces

[1] Barr also induces infringement of claim 6 of the '573 patent merely by inducing patients to use a product that it knows or should know falls within the scope of claim 6.

of . . . the frontal sinus," (iii) "allowing said sprayed composition to deposit on said surfaces," (iv) "in the form of a viscous composition," (v) "which resists being cleared from the mucosal surfaces by the inherent mucociliary forces which are present in the nasal cavity."

7. With respect to the undisputed terms, Dr. Eli Meltzer testified, without rebuttal by Barr, that Barr's ANDA product is "odorless" as required by claim 6 of the '573 patent. (Tr. 319-20; PTX 1). Similarly, Dr. Robert Lochhead testified, without rebuttal by Barr,[2] that testing according to the method described in the patents established Barr's ANDA product has an unsheared viscosity within the claimed range of about 400 to about 800 centipoise, and a viscosity when subjected to shear within the claimed range of about 50 to about 200 centipoise. (Tr. 200; PTX 355, 484). Dr. Lochhead also verified the accuracy of his viscosity testing protocol by testing the setting and shear viscosities of Nasacort® AQ as a control (Tr. 200, 791).

B. Barr's ANDA Product is Thixotropic Because It Returns to Its Unsheared Viscosity in Deposited Form

8. Plaintiffs demonstrated by more than a preponderance of the evidence that the viscosity of Barr's ANDA product "in deposited form on the mucosal surfaces" is about 400 to about 800 cp as required by claim 6 of the '573 patent. When deposited in the nose, Barr's ANDA product is in relatively unstressed form (Tr. 266-67; PTX 1), but its viscosity cannot be measured directly. (Tr. 262-63; PTX 363). Regardless, an understanding of thixotropic materials in general, and the rapid network-rebuilding capability of the Avicel suspending agent in Barr's ANDA product in particular, indicates that the viscosity of Barr's ANDA product in deposited form returns to its unsheared viscosity of about 400 to 800 centipoise. (Tr. 263).

9. Moreover, both the "Hydan Report" (PTX 365) and the "FMC Report" (PTX 380) independently indicate that the viscosity of Barr's ANDA product in deposited form returns to its

[2] Although fully able to do so, Barr's rheology expert, Dr. Daniel Klingenberg, did not perform any viscosity testing on Barr's ANDA product. (Tr. 516).

unsheared viscosity of about 400 to 800 cP. (Tr. 263).[3] Figure 2 of the Hydan report mimics the as-deposited low-stress state that occurs when Nasacort® AQ is sprayed on a surface (Tr. 255), and shows that Nasacort® AQ's viscosity rebuilds quickly after being sheared. (Tr. 267; PTX 365). Similarly, the FMC Report shows that the structure of Nasacort® AQ rebuilds quickly after being sprayed. (Tr. 252-53, 288; PTX 380). Given the compositional identity between Barr's ANDA product and Nasacort® AQ (Tr. 256), both reports support that Barr's ANDA product would return to its unsheared viscosity quickly after being deposited. (Tr. 256, 263-64).

10. Barr presented no evidence showing that the viscosity of Barr's ANDA product falls outside of the range of about 400 to about 800 cp when deposited on the mucosal surfaces. Instead, Barr's experts merely hypothesized that the deposited form viscosity might fall outside that range due to temperature effects, ciliary shear forces, or dilution by nasal secretions. (Tr. 410-16). However, temperature differences have essentially no effect on the rheology of Avicel-containing materials, like Barr's ANDA product. (Tr. 275). Also, the ciliary shear forces present in the nose would have essentially no effect on the viscosity of materials deposited on the mucous layer. (Tr. 275, 292). The mucous layer remains intact during ciliary transport (Tr. 86-87), and there is no evidence to indicate that ciliary action reaches or affects materials deposited thereon. Additionally, nasal secretions are unlikely to dilute and affect the viscosity of Barr's ANDA product. (Tr. 292-93).

11. Accordingly, Aventis has demonstrated by a preponderance of the evidence that the viscosity of Barr's ANDA product "in deposited form on the mucosal surfaces," is within the claimed range of about 400 to about 800 centipoise. For similar reasons, to the extent that claim 26 of the '329 patent is construed to additionally include that the viscosity of Barr's ANDA

[3] Those reports were prepared prior to this litigation; the Hydan Report was commissioned by the manufacturer of Barr's ANDA product.

product in deposited form is relatively high such that it resists being cleared from the mucosal surfaces by the inherent mucociliary forces which are present in the nasal cavity, Aventis has also demonstrated this element by a preponderance of the evidence. (Tr. 145-47, 201-02, 250-56, 261-64, 266--70, 516; PTX 48, 362, 365, 380).

C. Barr's ANDA Product Deposits on All of the Mucosal Surfaces

12. The preponderance of the evidence further shows that Barr's ANDA product deposits on the mucosal surfaces, including the frontal sinus, as required by the asserted claims. During trial, Dr. Marc Berridge discussed the results of a pre-litigation January 4, 1996 PET study he conducted using radiolabeled Nasacort® AQ to determine the deposition and kinetics of the drug when used according to the package insert in human volunteers. (PTX 528; Tr. 121-23). This 1996 PET study showed that Nasacort® AQ deposited in the anterior regions of the nose (Tr. 132), the turbinate regions (Tr. 133), the maxillary sinuses (Tr. 133-34), and the frontal sinus (Tr. 134-35) for all of the volunteers in the 1996 study. In fact, as admitted by Dr. Barry Siegel testifying on behalf of Barr, the values shown in the frontal sinus for the 1996 volunteers were very similar to those shown in the maxillary sinuses for these same volunteers. (*Id.*, Tr. 470-471; PTX 528). Further, Dr. Berridge testified that 3 of 5 subjects in his 1998 PET study of Nasacort® AQ similarly showed deposition in all of the claimed regions of the nasal cavity, including the frontal sinus. (Tr. 139-41; PTX 569).

13. In support of the reliability of the 1996 PET Study, Dr. Berridge testified that great care was taken not to assign a cubic region to the frontal sinus if that cubic region had a chance of including data from an adjacent anatomical region. (Tr. 128-129). Apart from the cubic regions, Dr. Berridge's subsequent studies on Nasacort® AQ all used the same protocols and methods of analysis. (Tr. 181). Further, the data from the 1996 Study was published in a respected peer-reviewed journal. (Tr. 153; 479).

14. Although he had the capabilities to do so (Tr. 475), Dr. Siegel never conducted PET testing of either Nasacort® AQ or Barr's ANDA product to support his opinion that there was no deposition in the frontal sinus (Tr. 474). Instead, Dr. Siegel relied almost entirely upon Dr. Berridge's 2002 PET study of Nasacort® AQ, ignoring the Results Summary of the 2002 Study Report stating that there were "unusual variations between observations from the individual subjects" in that study. (PTX 351; Tr. 172-173; Tr. 485-487).

15. Tellingly, while several of Barr's experts expressed opinions as to the difficulties of deposition on the frontal sinus, Aventis is the only party that proffered actual data on this issue in the form of Dr. Berridge's PET studies. (Tr. 474-475). Furthermore, Dr. Michael Kaliner established that Barr's experts' opinions were flawed. (Tr. 82-83, 698-706). Accordingly, the 1996 and 1998 PET studies establish that Nasacort® AQ, and thus Barr's ANDA product, deposits on the mucosal surfaces of the nasal cavity as required by the asserted claims. (Tr. 143-145).

D. Barr's ANDA Product Resists Mucociliary Clearance

16. The preponderance of the evidence shows that Barr's ANDA product resists being cleared from the mucosal surfaces by the inherent mucociliary forces which are present in the nasal cavity, as required by the asserted claims. It is known that standard mucociliary clearance clears materials from the nose very rapidly, within ten to thirty minutes. (Tr. 88-89; 146). The data from the 1996 PET study, which was confirmed by Dr. Siegel (Tr. 469-471), showed that Nasacort® AQ was retained for about an hour in the anterior regions of the nose (Tr. 133), the turbinate regions (Tr. 133), the maxillary sinuses (Tr. 133-134) and the frontal sinus (Tr. 134-135).

17. Barr presented no evidence showing that Nasacort® AQ was not retained for about an

hour or did not resist mucociliary clearance. Accordingly, Nasacort® AQ, and thus Barr's ANDA product, resists being cleared from the mucosal surfaces by the inherent mucociliary forces present in the nasal cavity, as required by the asserted claims.

III. THE ASSERTED CLAIMS OF THE '573 AND '329 PATENTS ARE VALID

A. Barr Has Not Presented Clear and Convincing Evidence That Aventis's Clinical Trials Were a Public Use Under 35 U.S.C. § 102(b)

18. A public use under § 102(b) is a "use of [the claimed] invention by a person other than the inventor who is under no limitation, restriction or obligation of secrecy to the inventor." *Netscape Commc'ns. Corp. v. Konrad*, 295 F.3d 1315, 1320 (Fed. Cir. 2002). Public use is evaluated in view of "the totality of the circumstances . . . in conjunction with the policies underlying the public use bar." *Id.*

19. The accused infringer must prove public use by clear and convincing evidence. *Netscape*, 295 F.3d at 1320. If a *prima facie* case of public use is established, then the patentee may come forward with evidence that the use was experimental. *Lough v. Brunswick Corp.*, 86 F.3d 1113, 1120 (Fed. Cir. 1996); *TP Labs., Inc. v. Prof'l. Positioners, Inc.*, 724 F.2d 965, 971 (Fed. Cir. 1984). However, questions of public use are often decided before reaching the question of experimental use – in a recent case, Barr made the same argument it made here and the court found that there was no *prima facie* case that Phase 3 clinical trials were public. *Bayer Schering Pharma AG v. Barr Labs., Inc.*, 2008 WL 628592 at *37-44 (D.N.J. March 3, 2008).

20. In this case, Barr argues that Aventis's clinical trials were a public use because (1) the patients did not sign a confidentiality agreement; and (2) the patients were allowed to take the study drug home with them.[4] Not only are these facts not dispositive, they fade in importance,

[4] Barr asserts that Aventis is precluded from arguing that the clinical trials were an experimental use because the trials occurred after reduction to practice. Reduction to practice, however, bears no relationship whatsoever to the *prima facie* case of public use. Moreover, Aventis disputes Barr's

particularly when the evidence shows that the use was otherwise restricted. *Bayer*, 2008 WL 628592 at *40-41 (noting that "lack of confidentiality provisions for the human patients is not outcome determinative on the public nature of the use" and finding adequate control over the study drug); *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 364 F. Supp. 2d 820, 912-13 (S.D. Ind. 2005), *aff'd* 471 F.3d 1369 (Fed. Cir. 2006); *Janssen Pharm. N.V. v. Eon Labs Mfg.*, 374 F.Supp.2d 263, 276 (E.D.N.Y. 2004), *aff'd* 134 Fed. Appx. 425 (Fed. Cir. 2005).

21. Moreover, Aventis presented a great deal evidence that it maintained tight confidentiality and control over the clinical trials. Every investigator in the clinical trials signed both an Investigator's Agreement that bound them to follow the detailed study protocols and a Confidential Disclosure Agreement. (Tr. 683-84, 689, 736-738; PTX 191, 425, 432-436, 438, 442). The protocols set forth patient inclusion and exclusion criteria, a specific study plan, study drug dispensing and storage procedures, and record-keeping procedures and imposed strict confidentiality restrictions on the investigators. (Tr. 685, 725-26, 727; PTX 425, 438). Pursuant to the study protocols and Federal law, the investigators closely monitored the dispensing and collected all study samples at the conclusion of a patient's involvement. (Tr. 685-86; PTX 425, 438). Furthermore, the investigators were not permitted to dispense any samples to patients outside of the clinical studies. (Tr. 733). Aventis regularly monitored the study sites during the clinical trials to ensure compliance with the protocols. (Tr. 734-36; PTX 194, 195).

22. RPR also controlled the activities of the patients enrolled in the clinical trials. First, RPR required patients to sign an informed consent form before receiving the study drug. (PTX 192 at NAQ0034252-301; PTX 440 at NAQ056214-43; Tr. 729). Pursuant to that form, only patients

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assertion. *See, e.g., Honeywell Int'l Inc. v. Universal Avionics Sys. Corp.*, 488 F.3d 982, 998 (Fed. Cir. 2007) (permitting experimentation after reduction to practice). *Cf. Atlanta Attachment Co. v. Leggett & Platt, Inc.*, 516 F.3d 1361, 1368-70, (Fed. Cir. 2008) (commenting on the confusion in the case law about the relationship between reduction to practice and experimental use) (Prost, J., concurring).

in the clinical studies were allowed to take the study drug. (*E.g.,* PTX 192 at NAQ0034256; Tr. 731) Additionally, RPR required patients to maintain a diary to record their daily use of the study drug. (*E.g.,* PTX 192 at NAQ0034240; PTX 440 at NAQ0056208; Tr. 686, 731:13 – 732). The patients were also required to make periodic visits to the investigators (*see* PTX 425 at NAQ0302933-37; PTX 438 at NAQ0056149-53), were provided only a very limited amount of the study drug (Tr. 674– 675, 747–748, 748), and were required to return any unused drug to the investigators. (PTX 192 at NAQ0034254; PTX 425 at NAQ0302950; PTX 438 at NAQ0056165; PTX 440 at NAQ0056215-16; Tr. 734). In addition, neither the investigators nor the patients knew any ingredients of the study drug besides the active ingredient and water. (*See* PTX 192, 425, 438, 440; Tr. 685, 728- 733). Neither the investigators nor the patients knew who was getting the study drug and who was getting placebo. (Tr. 675, 687, 729-30, 732-33; PTX 196). Accordingly, neither the investigators nor the patients were aware of the formulation or its innovative features. *See Bayer*, 2008 WL 628592, at *41; *Janssen*, 374 F.Supp.2d at 276. Aventis's clinical trials were thus not a public use under § 102(b).

B. Barr Has Not Presented Clear and Convincing Evidence That the '573 and '329 Patents were Obvious

23. Barr bears the burden of showing by clear and convincing evidence that each of the asserted claims is invalid over the prior art due to obviousness. 35 U.S.C. § 103. In doing so, Barr must establish that the prior art taught the subject matter of the asserted claims as a whole, as those claims were construed by the Court. The burden on Barr is especially great in a case like this, where the art alleged to invalidate the patent claims were the very same references that were before the examiner when the claim was allowed. *Ultra-Tex Surfaces, Inc. v. Hill Bros. Chem. Co.*, 204 F.3d 1360, 1367 (Fed. Cir. 2000) (quoting *American Hoist & Derrick Co. v. Sowa & Sons, Inc.*, 725 F.2d 1350, 1359 (Fed. Cir. 1984).

1. Barr Failed to Apply the Proper Obviousness Analysis

24. Barr failed to compare the prior art to the properly-construed claims, as is required. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1576 (Fed. Cir. 1987). Specifically, instead of applying the definition of "thixotropic" provided by the Court, Barr's expert on obviousness issues, Dr. Thomas Needham, admitted that he applied a general definition. (Tr. 637-42). As Dr. Needham testified,

> Q: So your testimony was that you did not use the Court's definition of thixotropic in your obviousness analysis. Is that a correct summary of your testimony?
>
> A: I think the –
>
> Q: Was that your testimony?
>
> A: That was my testimony.

(Tr. 641). Barr therefore failed to establish a *prima facie* case of obviousness because it did not establish that any prior art reference described a "thixotropic" product.[5]

25. Similarly, Barr presented no evidence that certain elements of the asserted claims were found in the prior art as a predicate to its obviousness analysis. *See, e.g.*, *Abbott Labs. v. Sandoz, Inc.*, 529 F. Supp. 2d 893, 916 (N.D. Ill. 2007). Dr. Needham admitted that he did not consider whether any prior art reference met the "exact viscosity numbers" required by the claims. (Tr. 641-44). In his obviousness determination, he did not use any information that would establish (i) the viscosity of any prior art product in unsheared form is about 400 to about 800 centipoise (Tr. 642-43); (ii) the viscosity of any prior art product is about 50 to about 200 centipoise as the composition is subjected to shear in preparation for spraying (Tr. 643-44); or (iii) in deposited

[5] Dr. Needham erred as well by using inappropriate documents as a basis for his analysis. Several documents were internal Aventis documents, and their contents would not have been known to those of ordinary skill in the art. (Tr. 645-47; DTX 33, 37). Others were not enabling, and therefore would not have been available for an obviousness analysis. *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551 (Fed. Cir. 1989). (Tr. 654; DTX 10, 11).

form on the mucosal surfaces, the viscosity of any prior art product is about 400 to about 800 centipoise (Tr. 644). In addition, Dr. Needham admitted that no nasal suspension product had ever used a chelating agent (such as EDTA, as required by the asserted claims) before the invention claimed in the patents. (Tr. 657-60). Because those elements of the asserted claims were absent from Barr's obviousness analysis, Barr failed to establish a *prima facie* case of obviousness.

2. The Evidence Adduced at Trial Shows that the Claimed Invention Was Not Obvious

26. The evidence at trial showed that the shear viscosity of Flonase when measured according to the method described in patents is between 307 and 375 centipoise, well outside the claimed shear viscosity range of 50-200 centipoise. (Tr. 788; PTX 484). Similarly, the shear viscosity of Beconase AQ is between 358 and 376 centipoise, again well also outside the claimed shear viscosity range. (Tr. 788; PTX 484).

27. Dr. Klingenberg's viscosity measurements for Flonase were unreliable because he altered his testing method in order to produce a shear viscosity within the claimed range. (Tr. 534-36; PTX 447). His protocol was similarly unreliable because it lacked any control; he never tested Nasacort® AQ to determine if his protocol produced the expected setting and shear viscosities. (Tr. 536-37). Thus, Barr has not presented clear and convincing evidence that either Flonase or Beconase AQ exhibited shear viscosities within the recited ranges, and therefore Barr failed to show that these products rendered the asserted claims obvious.

28. The evidence strongly supports that other elements of the asserted claims are missing from the prior art as well. As Dr. Eli Meltzer testified, prior art products such as Beconase AQ, Vancenase AQ, and Flonase are not "odorless" under the Court's definition. (Tr. 799-800, 802-13). Dr. Ian Mackay admitted that those products would cause user discomfort – and therefore

not be "odorless" – if they caused nasal irritation or burning, or if clinical study participants dropped out because of nasal irritation.[6] (Tr. 370-72). Dr. Mackay recognized that the package insert indicated that Flonase causes nasal irritation and burning, and that clinical study participants dropped out because of nasal irritation; nasal irritation is also one of the reported adverse effects of Beconase AQ and Vancenase AQ. (Tr. 369-71; PTX 758, 759). In contrast, nasal irritation is not one of the reported adverse effects of Nasacort® AQ. (Tr. 653-54; PTX 374). Thus, none of the prior art products cited by Barr was "odorless," and that element was missing from the prior art.

29. Also, the prior art taught away from the claimed invention. *See Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 885 (Fed. Cir. 1998). As Dr. Needham admitted, his own publications (which cited numerous other articles) indicated that a person of ordinary skill in the art would have thought increased viscosity would prolong retention time, but would have understood that it would not be predictable. (Tr. 632-36; PTX 1062, 1063). The viscosity of Flonase is higher than that of Nasacort® AQ, Barr's ANDA product, and the viscosity ranges required by the claims. (Tr. 636; 787-91; PTX 1, 3, 365, 484). Furthermore, the same publications indicated that products having suitable viscosity requirements could be formulated, but "would not be easily administered to the nasal cavity with the existing drug delivery devices," such as spray pumps. (Tr. 632-33; PTX 1062, 1063). Finally, Dr. Needham testified a person of ordinary skill in the art would not have pursued the path of a product that caused irritation or burning, which Beconase AQ, Vancenase AQ, and Flonase all do. (Tr. 652-54; PTX 758, 759). Thus, the prior art would have taught away from the claimed invention.

[6] Dr. Mackay testified that he believed Flonase was odorless because none of his patients had complained about the odor. (Tr. 359-60). However, Dr. Mackay had *never* asked any patient whether the smell of an intranasal steroid product was causing them discomfort. (Tr. 369-70).

3. Secondary Considerations Show the Claimed Invention Was Not Obvious

30. The claimed invention is also not obvious because numerous secondary considerations suggest otherwise. Secondary considerations must be considered in any case in which they are present. *WMS Gaming Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983) ("[E]vidence of secondary considerations may often be the most probative and cogent evidence in the record"). In this case, Aventis has demonstrated the existence of secondary considerations including unexpected results, failure of others, copying of the invention, long-felt need, and commercial success.

31. Unexpectedly, the claimed invention satisfied a long-felt need for a safe intranasal steroid spray that did not have sensory attributes that caused patients to refuse to comply with their prescribed treatment regimen. Like predecessor products, Beconase AQ, Vancenase AQ, and Flonase caused unacceptable systemic side effects – growth inhibition in children for Beconase AQ and Vancenase AQ, adrenal suppression for Flonase. (Tr. 314-16, 381-83; PTX 375, 1060, 1061).[7] Certain physicians stopped prescribing Beconase AQ and Vancenase AQ because of those effects. (PTX 582). In contrast, Nasacort® AQ has no systemic side effects. (Tr. 381). Beconase AQ, Vancenase AQ, and Flonase all should have been more potent than Nasacort® AQ but, inexplicably, they are not. (Tr. 384, 696-97; PTX 391, 443). Nasacort® AQ was also preferred by subjects in clinical trials because of its sensory attributes, and the patients indicated that they would be more likely to comply with a treatment regimen of Nasacort® AQ than Beconase AQ, Vancenase AQ, and Flonase because of the distinction in sensory attributes. (Tr.

[7] The unacceptable side effects may have been due to the preservative system of phenylethyl alcohol and benzalkonium chloride, which increases bioavailability, perhaps through ciliotoxicity (Tr. 658-60; PTX 1062). Nasacort® AQ does not have cilitoxic phenylethyl alcohol in its formulation (Tr. 660-62; PTX 262)

809-810; PTX 393, 394, 408, 409). Those same sensory attributes were some of the ones that had caused allergy patients to quit following their prescribed regimens for other nasal sprays, according to the extensive Allergies in America survey. (Tr. 374-78, 827-28; PTX 1059).

32. Nasacort® AQ has been a commercial success, and its success has been linked to the merits of the patented invention. Nasacort® AQ has had U.S. sales of over $2 billion since its 1996 launch. (Tr. 754-56). The market share of Nasacort® AQ has increased over time, growing at an average rate more than twice the growth rate of the market as a whole. (Tr. 754, 756-57). Growing demand for Nasacort® AQ has occurred despite supply interruptions, showing that physicians continually have wanted to prescribe, and patients continually have wanted to use, the product. (Tr. 754, 757-58). Finally, sales of Nasacort® AQ have generated substantial profits for Aventis, covering far more than the costs of production and marketing (Tr. 754-55, 758-60). More to the point, if Nasacort® AQ were not sucessful, why would Barr want to copy it? *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 2001 WL 1397304 at *12 (S.D. Ind. Oct. 29, 2001) ("If the patented drug were not a commercial success, generic manufacturers would have little interest in offering their own versions of the drug.").

33. The commercial success of Nasacort® AQ is tied to the claimed elements of the invention. A "*prima facie* case of nexus is generally made out when the patentee shows both that there is commercial success, and that the thing (product or method) that is commercially successful is the invention disclosed and claimed in the patent." *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988). Beyond that unrebutted presumption, Aventis has shown that the marketing of Nasacort® AQ is and has been based on the patented features, and that Nasacort® AQ's success has not been due to excessive marketing expenditures or an inordinately low price as compared to the rest of the market. (Tr. 760-69).

34. Barr did not contest that several other secondary considerations exist. Another company, Muro, attempted to design around the claimed invention and had failed. (Tr. 801-02). Muro's product used a co-solvent TAA system, but had problems with nasal stinging and was withdrawn from the market because of stability problems. (*Id.*; PTX 398, 402, 984). In addition, Barr admitted that it copied the exact formulation of Nasacort® AQ from the patents. (Tr. 34-35; Zeevi Deposition Transcript (62:19-63:4; 63:7-63:10; 67:15-67:23; 67:25-68:5; 68:7-68:8; 79:21-79:24; 80:1-80:6)). And Barr did not contest that Nasonex copied the odorless formulation of Nasacort® AQ because of the same sensory studies that prove prior art products are not odorless. (Tr. 810-12; PTX 412).

C. The Specification of the '573 and '329 Patents Enables the Claimed Invention

35. Barr failed to show by clear and convincing evidence that the specification of the '573 and '329 patents fails to enable one of ordinary skill in the art to make a product that meets the limitations of depositing on the mucosal surface of the frontal sinus and resisting being cleared from the mucosal surfaces by the inherent mucociliary forces which are present in the nasal. Whether the specification enables one skilled in the art to make and use the claimed invention without undue experimentation is determined as of the filing date of the application, July 3, 1996. (D.I. 163 (Appendix A, ¶¶ 8, 10)); *see Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991). As described above, not only has Aventis enabled these claim elements through Nasacort® AQ, but Barr's ANDA product falls within the scope of these claim limitations.

IV. CONCLUSION

36. For the forgoing reasons, the Court finds the asserted claims infringed and valid.

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